

EXHIBIT F

7. Rolipram is referred to as a prototypical PDE4 inhibitor. This means that people in the field view results obtained by using it as representative for results obtained using other PDE4 inhibitors. Table 2 of Teixeira et al. describes in detail a number of PDE4 inhibitors, and confirms their functional similarity. Teixeira et al., Trends in Pharm. Sci. 18:164-71.

8. Because of the functional similarity of the PDE4 inhibitors, I was confident that once I had demonstrated that rolipram was an efficacious treatment for CLL, other PDE4 inhibitors would also be useful to treat CLL. My studies with the PDE4 inhibitor Ro20-174 confirmed this finding. The data for both of these PDE4 inhibitors is included in the specification.

9. My results have been further confirmed by my studies of the treatment of CLL with a third PDE4 inhibitor. One set of my experiments is represented in the graph below. In this experiment, apoptosis was analyzed in CLL cells exposed to increasing concentrations of a PDE4 inhibitor in the presence or absence of 40 micromolar forskolin.

10. These results show that another PDE4 inhibitor can treat CLL as taught.

